

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
11 October 2001 (11.10.2001)

PCT

(10) International Publication Number  
WO 01/74300 A1

(51) International Patent Classification<sup>7</sup>: A61K 6/00, 7/00,  
9/70, A61F 13/00, A61L 15/16, 15/00

(21) International Application Number: PCT/US01/08741

(22) International Filing Date: 16 March 2001 (16.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/538,655 30 March 2000 (30.03.2000) US

(71) Applicant: BRENNEN MEDICAL, INC. [US/US]; 1290  
Hammond Road, St. Paul, MN 55110 (US).

(72) Inventors: KLEIN, Barbara; 27 Raven Road, North  
Oaks, MN 55127 (US). KATZNER, Leo, D.; 2460 Emer-  
ald Lane, Shakopee, MN 55379 (US).

(74) Agent: MCLAUGHLIN, Christopher, J. Moore &  
Hansen; 2900 Wells Fargo Center, 90 South Seventh  
Street, Minneapolis, MN 55402 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,  
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

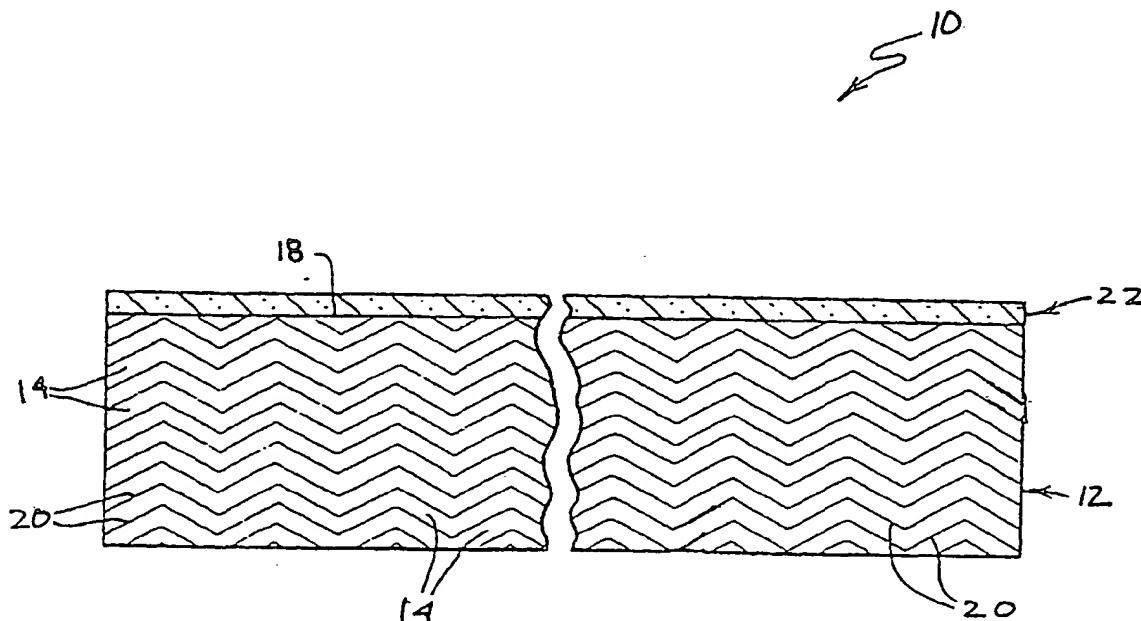
(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: ANTI-MICROBIAL AND IMMUNOSTIMULATING COMPOSITION



(57) Abstract: A medical composition comprising an immunostimulating agent such as a  $\beta$ -glucan compound and an anti-microbial agent such as a silver compound is disclosed. The medical composition may be adapted for use topically or as part of a mesh matrix which may be further adapted for use as a wound dressing or as a surgical mesh.

WO 01/74300 A1

## ANTI-MICROBIAL AND IMMUNOSTIMULATING COMPOSITION

### *Background of the Invention*

This invention relates generally to an antimicrobial and immunostimulating medical composition which may be adapted for use topically or as part of a mesh  
5 matrix which may be further adapted for use as a wound dressing or as a surgical mesh.

It is known to utilize immunostimulating agents as components of topical compositions, wound dressings, and surgical meshes. Examples of these uses are given in U.S. Patent 5,980,918 to Klein, U.S. Patent No. 5,676,967 to Williams *et al.*,  
10 and U.S. Patent Application Serial Number 09/406,551 also to Klein, respectively. U.S. Patent Nos. 5,980,918 and 5,676,967, and U.S. Patent Application 09/406,551 are all assigned jointly with the present application and are hereby incorporated by reference.

There is a need with respect to all topical compositions, wound dressings and  
15 surgical meshes to provide an effective anti-microbial function in addition to the immunostimulating function described above.

This and other objectives and advantages of the invention will appear more fully from the following description, made in conjunction with the accompanying drawings wherein like reference characters refer to the same or similar parts  
20 throughout the several views.

***Brief Summary of the Invention***

It is the objective of this invention to provide an improved medical composition that has the immunostimulating properties common to the topical compositions, wound dressings, and surgical meshes described in the aforementioned patents and patent application, along with anti-microbial properties that aid in preventing or alleviating infection. Consequently, a medical composition according to the present invention comprises an immunostimulating agent such as a  $\beta$ -glucan compound and an anti-microbial agent such as a silver compound.

Preferably the medical composition of the present invention includes a cereal derived  $\beta$ -glucan derived from one of wheat, oats, and barley. The silver component of the medical composition is preferably chosen from a group comprising elemental silver, silver nitrate, silver bromide, silver sulfate, silver fluoride, silver iodide, silver chloride, silver oxides, silver protein, silver lactate, silver citrate, and silver sulfadiazine.

A topical composition formulated according to the principles of the present invention may take the form of a an unguent, a cream, a gel, an emollient, an oil or a lotion. A specific formulation of a topical composition comprising the medical composition of the present invention and taking the form of a lotion may include 0.05 - 15 w/w % oat-derived Beta-d-glucan and 0.05 - 15 w/w % Silver nitrate. Additional components may include: 20-90 w/w % Water, 3-60 w/w % petrolatum, 2-30 w/w % glycerol stearate, and 2-20 w/w % PEG 100 stearate.

Another formulation of a topical composition for application to the skin and mucosa for treating burns and wounds and other skin loss injuries and conditions comprises 0.05-15 w/w %  $\beta$ -D-glucan and a silver compound as active ingredients in

one of a cream base, gel base and oil base. The  $\beta$ -D-glucan is preferably derived from oats, wheat or barley, but may also be derived from yeast, bacteria, and fungus. An especially beneficial form of  $\beta$ -D-glucan is characterized as (1 $\rightarrow$ 3)(1 $\rightarrow$ 4)  $\beta$ -D-glucan and is derived from of the aforementioned oats, wheat, and barley.

5 Another formulation of a topical composition comprising the medical composition takes the form of a cream and includes  $\beta$ -glucan, a solvent including water, an ointment base, an emulsifying/solubilizing agent, a suspending/viscosity increasing agent, and a preservative agent. Preferably, the solvent of this formulation will comprise at least 20 w/w % of the topical composition. The solvent may include  
10 an emollient such as glycerol or propylene glycol. The ointment base typically makes up 3 – 60 w/w % of the topical composition and may comprise petrolatum, cod liver oil, mineral oil, shark oil, paraffin, lanolin, cetyl alcohol, and/or cetyl ester wax.

A stiffening agent useful in forming a topical composition with the medical composition of the present invention may comprise cetyl alcohol, cetyl esters wax,  
15 and paraffin. A suitable emulsifying/solubilizing agent may be selected from a group including sodium lauryl sulfate and non-ionic emulsifiers such as glyceryl stearate, PEG 100 stearate and triethanolamine. A suspending/viscosity increasing agent suitable for use with the medical composition is selected from the group comprising polyvinyl alcohol, agarose, alginate, xanthan gum, guar gum, sodium  
20 carboxymethylcelluloses, and carbomer. A preservative agent selected from the group comprising methyl paraben, ethyl paraben, butyl paraben, propyl paraben, benzalkonium chloride, imidurea, and diazolidinyl urea may also be used in a topical composition formulated according to the present invention.

In order to formulate a gel with the medical composition of the present invention a gel base including water, at least one suspending/viscosity increasing agent, and optionally a preservative agent may be mixed with the medical composition. The suspending/viscosity increasing agent(s) is typically chosen from a group that includes polyvinyl alcohol, sodium carboxymethylcellulose, xanthan gum, agarose, alginate, guar gum, and carbomer. The suspending/viscosity increasing agent(s) may include one or more of the aforementioned group. Such a gel preferably has a water base including at least about 50 w/w percent water. More specifically, such a gel may comprise about 50-98 w/w % water and about 0.5-15 w/w % suspending/viscosity increasing agent(s).

The medical composition of the present invention may form a layer of a biocompatible surgical mesh or may be impregnated into a mesh matrix of such a surgical mesh. Similarly, the medical composition may also form a layer of a wound dressing or may be impregnated into a mesh material of a wound dressing.

The materials from which biocompatible surgical meshes that include the medical composition of the present invention may be fabricated are preferably chosen from a group that includes polyester polypropylene, polytetrafluoroethylene, expanded polytetrafluoroethylene, polyethylene terephthalate, polyglycolic acid, polyglactin, and dacron-polyethylene reinforced silicone. Suitable organic biocompatible surgical meshes that may be combined with the medical composition of the present invention may be derived from human sources, animal sources, and cadaveric sources.

A wound dressing comprising the medical composition of the present invention may include a mesh material that has a coating that includes a  $\beta$ -glucan

compound and elemental silver or a silver compound. Additional components of the wound dressing may include a coating of a collagenic protein and a polymeric film that is applied to one side of the coated mesh material. The  $\beta$ -glucan of the medical composition is applied to the mesh material of the wound dressing to produce a concentration equal to about 0.01-15 percent of the dressing's dry weight. The optional collagenic protein component of the wound dressing comprises a mixture of Type I and Type III collagens that makes up 0.1-20 percent of the dry weight of the dressing. The polymeric film that is applied to the wound dressing is preferably a high vapor permeable material.

Another embodiment of a wound dressing which incorporates the medical composition of the present invention may comprise a polyester mesh netting formed of a woven monofilament polyester having a thickness of about 0.01-0.05 inches. To this netting is applied a coating that includes a  $\beta$ -glucan compound and a silver compound that are mixed with a collagenic protein in a ratio of 1:100 to 100:1 on a dry weight basis. Finally, a polymeric film of high vapor permeable material is bonded to one side of the coated mesh netting to comprise an exterior surface of the wound dressing.

### ***Brief Description of the Drawings***

Figure 1 is a side view of a wound dressing incorporating the medical composition of the present invention; and,

Figure 2 is a side view of a surgical mesh incorporating the medical composition of the present invention.

## ***Description of the Preferred Embodiments***

### **Medical Composition**

The preferred active ingredients of the medical composition of the present invention are a  $\beta$ -glucan compound and a silver compound. Compounds classified as  $\beta$ -glucans comprise a large group of higher molecular weight polymers containing glucopyranosyl units in  $\beta$ -linked chains.  $\beta$ -glucans are found in essentially all living cells that are enclosed by cell walls and have considerable structural variation depending on the source.  $\beta$ -glucans are highly unbranched homopolysaccharides and are isomerically disposed to  $\alpha$ -D-glucan (e.g. starch), which is typically non-functional as a structural support component of the cell. Various types of  $\beta$ -glucans are described in U.S. Patent No. 5,980,918 to Klein, which was incorporated by reference above. The most readily available types of  $\beta$ -glucans are those derived from yeast, bacteria, fungi and from cereal grains such as wheat, barley, and oats. All of these  $\beta$ -glucans may be used to formulate the medical composition of the present.

As described in U.S. Patent 5,980,918,  $\beta$ -glucans have a strong immunostimulating property, which makes them ideal for use in medical compositions applied to wounds and surgical sites. The  $\beta$ -glucans actually stimulate the immune response of the tissues at the wound or surgical site, which has the effect of improving tissue regeneration and speeding recovery. As further described in U.S. Patent 5,980,918, cereal derived  $\beta$ -glucans have been shown to be the most efficacious in stimulating the immune response of the tissues at a wound or surgical site. Therefore, it is preferred to utilize cereal derived  $\beta$ -glucans such as those derived from wheat, barley and oats as the immunostimulating component of the medical composition of the present invention.

The second active ingredient of the medical composition of the present invention is a silver compound having antimicrobial properties. Silver compounds of the type to be used with the medical composition of the present invention act to kill or inhibit the growth of bacteria or other infectious agents that may be present at a wound or surgical site. Silver compounds suitable for use with the medical composition of the present invention comprise elemental silver, the inorganic silver salts, i.e. silver nitrate, silver bromide, silver sulfate, silver fluoride, silver iodide, silver chloride and silver oxides, and the organic silver salts such as silver protein (mild and strong), silver lactate, silver citrate, or silver sulfadiazine. It is to be understood that this is not an exhaustive list of the silver compounds which may be used with the medical composition of the present invention and that additional silver compounds may be used.

It should be understood that other antimicrobial compounds comprising zinc or similar metals may also be used in the medical composition of the present invention either in place of, or in combination with a silver compound.

#### Topical Compositions

The medical composition of the present invention may comprise a component of a topical composition of the type described in U.S. Patent No. 5,980,918. In use, such a topical composition is preferably applied directly to a wound or to a surgical site so that the immunostimulating and anti-microbial properties of the topical composition may work in conjunction to stimulate healing. A topical composition which comprises the medical composition of the present invention may be formulated in various ways including those topical composition variously known as unguents, creams, gels, emollients, lotions and oils, each with a generally



characteristic solvent composition and having a form ranging from liquid to semi-solid. By way of example, and without limiting the forms that a topical composition comprising the medical composition of the present invention may take, a specific formulation of a lotion comprising the medical composition of the present invention is  
5 described hereinbelow.

An aqueous solution of oat derived  $\beta$ -glucan was prepared by dissolving 2 grams of oat derived  $\beta$ -glucan in 165 grams of water at 95 degrees Celsius. A separate oil phase solution was prepared by mixing 20 grams petrolatum with 10 grams of a glycerol stearate (49%)/PEG 100 stearate (51%) blend. This blend may  
10 be replaced by equal amounts of the respective constituents or by an equivalent compound. The oil phase solution was heated to 65 degrees Celsius and added to the aqueous solution which had been cooled to, and held at, 65 degrees Celsius. The mixture of the oil phase and aqueous solutions was emulsified for two minutes at 27000 RPM in a mixer. Three grams of silver nitrate were then added and  
15 emulsification continued for an additional one minute. The weight percentages (w/w %) of the components of the prepared lotion were as follows:

Beta-d-glucan (oat derived)	1%
Silver nitrate	1.5%
Water	82.5%
20 Petrolatum	10%
Glycerol Stearate	2.5%
PEG 100 Stearate	<u>2.5%</u>

Total

100%

## Wound Dressing

The medical composition of the present invention may be used in fabricating wound dressings that have both immunostimulating and anti-microbial properties.

5 The medical composition of the present invention may be added to a mesh matrix wound dressing 10 of the type disclosed in U.S. Patent No. 5, 676,967 to Williams, *et al.* incorporated by reference above. In such a wound dressing, the medical composition containing a  $\beta$ -glucan compound and a silver compound would be used to impregnate a mesh netting material 12 such as that illustrated in Figure 1. The

10 mesh netting material is preferably a multifilament woven mesh formed of thin polyester fibers 20, though it is important to point out that other types of meshes may be used, including but not being limited to gauzes, synthetic meshes, and organic meshes (of both autologous and homologous sources). The mesh netting material 12 has a structure with holes or openings 14 that permit a solution containing the

15 medical composition of the present invention to impregnate the mesh netting material 12. The impregnated mesh netting may also comprise a vapor permeable layer 22, which is occlusive to moisture and bacteria. The vapor permeable layer of butylene/poly(alkylene ether) phthalate plus stabilizer is joined to surface 18 of the mesh netting material 12 by a thermal process or other means and acts to prevent

20 moisture and bacteria from entering the wound while allowing vapor to pass through the dressing 10 from the wound site into the air.

An example of a wound dressing which comprises the medical composition of the present invention is described herein below. A aqueous solution of oat derived  $\beta$ -glucan and silver nitrate was prepared. The solution contained 1.0 weight percent  $\beta$ -

glucan and 0.3 weight percent silver nitrate. This aqueous solution was used to impregnate the mesh netting of the dressing. The aqueous solution in the mesh netting of the dressing was then dehydrated at 25 degrees Celsius. Following dehydration, the completed wound dressing with the impregnated mesh netting was  
5 packaged and sterilized. The weight percentages of the compounds of the resulting exemplary wound dressing were as follows:

	Beta-d-glucan (oat derived)	31.3%
	Silver nitrate	9.8%
	Mesh netting	<u>58.9%</u>
10	Total	100%

#### Surgical meshes

The medical composition of the present invention may also be used in producing surgical meshes of the type used in making structural repairs at a surgical site. Examples of surgical meshes incorporating a  $\beta$ -glucan compound are given in  
15 U.S. Patent Application Serial No. 09/406,551 to Klein, incorporated by reference above. Surgical meshes typically take the form of porous, gauze like sheets of material 30, which may be made from various organic materials (of both autologous and homologous sources) and synthetic materials. Common uses of surgical meshes include the repair of herniations and use as a structural member in  
20 gynecological surgeries. Preferably, the medical composition of the present invention will be used to impregnate a surgical mesh in the same manner as described above for the wound dressing 10 in conjunction with Figure 1. However, as illustrated in Figure 2, it is also possible that the medical composition may be a constituted as a

film that is applied as a discrete layer 32 to one or both sides of the surgical mesh 28 by a thermal process or by other means.

#### Zone of Inhibitions Study

A standard zone of inhibitions study was performed on the lotion and wound dressing exemplars described above. The zone of inhibition test involved placing a quantity of the prepared lotion or wound dressing in a petri dish, which had been cultured with a particular bacterium. The bacteria used in this test included: *B. subtilis*, *B. vulgatus*, *C. albicans*, *E. coli*, *P. aeruginosa*, and *S. aureus*. In each of these tests, the diameter of the prepared lotion or wound dressing placed in the cultured petri dishes was measured and recorded at the outset of the test. On the first, second, and fifth days thereafter the diameter of the zone of inhibition was measured and recorded. The zone of inhibition in this test was defined as the area surrounding the prepared lotion or wound dressing on the petri dish which was uninhabited by the bacteria of the specific culture. Table I reports data for the prepared lotion zone of inhibition test and Table II reports data for the prepared wound dressing zone of inhibition test.

**Table I  $\beta$ -glucan & Silver Lotion**

Bacterium	Measurement (cm)	Day 1	Day 2	Day 5
<i>B. subtilis</i> 1)	2.05	2.93	2.88	2.75
2)	2.20	2.90	2.93	2.90
Mean	2.13	2.92	2.91	2.83
<i>B. vulgatus</i> 1)	2.18	*	3.35	3.38

2)	2.15	*	3.45	3.40
Mean	2.17	*	3.40	3.33
<i>C. albicans</i> 1)	2.35	*	3.70	3.70
2)	2.23	*	3.55	3.65
Mean	2.29	*	3.63	3.68
<i>E. coli</i> 1)	2.05	2.78	2.78	2.68
2)	2.18	2.75	2.70	2.65
Mean	2.12	2.77	2.74	2.67
<i>P. aeruginosa</i>				
1)	2.13	3.08	3.03	3.03
2)	2.15	3.00	3.00	3.00
Mean	2.14	3.04	3.02	3.02
<i>S. aureus</i> 1)	2.10	3.08	3.08	3.05
2)	2.25	3.05	3.05	3.03
Mean	2.18	3.07	3.07	3.04

Table II -  $\beta$ -glucan & Silver Wound Dressing

Bacterium	Measurement (cm)	Day 1	Day 2	Day 5
<i>B. subtilis</i> 1)	2.30	3.33	3.35	3.30
2)	2.13	3.08	3.03	2.98
Mean	2.22	3.21	3.19	3.14
<i>B. vulgatus</i> 1)	2.43	*	4.13	3.98
2)	2.38	*	4.25	3.93
Mean	2.41	*	4.19	3.96
<i>C. albicans</i> 1)	2.23	*	3.88	3.90
2)	2.20	*	3.88	3.88
Mean	2.22	*	3.88	3.89
<i>E. coli</i> 1)	2.43	3.10	3.10	2.95
2)	2.63	2.98	2.95	2.90
Mean	2.53	3.04	3.03	2.93
<i>P. aeruginosa</i> 1)	2.20	3.33	3.35	3.28
2)	2.23	3.25	3.32	3.33
Mean	2.22	3.29	3.34	3.31

<i>S. aureus</i> 1)	2.15	3.30	3.30	3.30
2)	2.10	3.25	3.25	3.20
Mean	2.13	3.28	3.28	3.25

In explaining the results of the zone of inhibition tests it is easiest to refer to a specific example of the tests. Referring first to Table I, it can be seen that two separate petri dishes were prepared and cultured with the *B. subtilis* bacterium. Into these prepared petri dishes were placed quantities of the prepared lotion having diameters of 2.05 centimeters and 2.20 centimeters, respectively. After one day, the diameter of the zone of inhibition for these petri dishes was 2.93 centimeters and 2.90 centimeters, respectively. On day two, the zones of inhibition for these lotion samples were 2.88 and 2.93 centimeters in diameter respectively. And on day five, the zones of inhibition for these lotion samples were 2.75 and 2.90 centimeters, respectively.

Referring next to Table II, two petri dishes were prepared and cultured with the bacterium *B. subtilis*. Into these prepared petri dishes were placed portions of a wound dressing treated comprising the medical composition having respective diameters of 2.30 and 2.13 centimeters. After one day, the zones of inhibition surrounding the samples of the wound dressing in each of the petri dishes were 3.33 and 3.08 centimeters respectively. After two days, the zones of inhibition surrounding the wound dressing samples were 3.35 centimeters and 3.03 centimeters,

respectively. And, after five days, the zones of inhibition surrounding the wound dressing samples were 3.30 and 2.98 respectively.

The results of the zone of inhibition tests are indicative of a strong anti-microbial quality in both the prepared lotion and the prepared wound dressing.

5        The invention described above may be embodied in other forms without departing from the spirit or essential characteristics thereof. The embodiments disclosed in this application are to be considered in all respects as illustrative and not restrictive. The scope of the invention is indicated by the appended claims rather than by the foregoing description and all changes, which come within the meaning  
10    and range of equivalency of the claims, are embraced therein.



**Claims**

What is claimed is:

- 1 1. A medical composition for application to wounds and to surgical sites  
2 comprising a  $\beta$ -glucan compound and one of elemental silver and a silver  
3 compound.
- 1 2. The medical composition of Claim 1 wherein the  $\beta$ -glucan compound is a  
2 cereal derived  $\beta$ -glucan.
- 1 3. The medical composition of Claim 1 wherein the  $\beta$ -glucan compound is  
2 derived from one of wheat, oats, and barley.
- 1 4. The medical composition of Claim 1 wherein the silver compound is one of  
2 elemental silver, silver nitrate, silver bromide, silver sulfate, silver fluoride,  
3 silver iodide, silver chloride, silver oxides, silver protein, silver lactate, silver  
4 citrate, and silver sulfadiazine.
- 1 5. The medical composition of Claim 1, wherein the medical composition is in  
2 the form of a layer of a wound dressing.

1 6. The medical composition of Claim 1 wherein the medical composition is  
2 impregnated into a mesh material of a wound dressing.

1 7. The medical composition of Claim 1 wherein the medical composition is in the  
2 form of a layer of a surgical mesh.

1 8. The medical composition of Claim 1 wherein the medical composition is  
2 impregnated into a mesh matrix of a surgical mesh.

1 9. The medical composition of Claim 1 wherein the medical composition is a  
2 component of a topical composition.

1 10. The medical composition of claim 9 wherein the topical composition is a non-  
2 aqueous ointment.

1 11. The medical composition of Claim 9 wherein the topical composition is one of  
2 a gel, a cream, and a lotion.

1 12. The medical composition of claim 9 wherein the medical composition takes  
2 the form of an ointment comprising:

3  $\beta$ -glucan 0.05 – 15 w/w%; and,

4 silver nitrate 0.05 – 15 w/w%.

1 13. The medical composition of claim 9 wherein the topical composition also  
2 includes a hydrocarbon base comprising 50 – 99.5 w/w% petrolatum.

1 14. The medical composition of claim 9 wherein the topical composition also  
2 includes a preservative agent comprising methyl paraben and propyl paraben.

1 15. The medical composition of claim 9 wherein the topical composition also  
2 includes a viscosity increasing agent comprising:

3 cetyl esters wax 0.1 – 15 w/w%;

4 paraffin 0.1-15 w/w%; and,

5 mineral oil 1 – 20 w/w%.

1 16. The medical composition of Claim 9 wherein the topical composition is a lotion  
2 comprising:

3  $\beta$  -glucan (oat derived) 0.05-15 w/w %; and,

4 Silver nitrate 0.05-15 w/w %.

1 17. The medical composition of Claim 16 wherein the topical composition is a  
2 lotion comprising:

3 Water 70 - 90 w/w %; and,

4 Petrolatum 3 - 60 w/w %.

1 18. The medical composition of Claim 17 wherein the topical composition is a  
2 lotion comprising:

3 Glycerol Stearate 2 - 30 w/w %; and,

4 PEG 100 Stearate 2 - 20 w/w %.

1 19. The medical composition of Claim 9 wherein the topical composition is a lotion  
2 comprising:

3 Beta-d-glucan (oat derived) 0.05 - 15 w/w %

4 Silver nitrate 0.05 - 15 w/w %

5 Water 20 - 90 w/w %

6 Petrolatum 3 - 60 w/w %

7 Glycerol Stearate 2 - 30 w/w %

8 PEG 100 Stearate 2 - 20 w/w %.

1 20. The medical composition for application to wounds and to surgical sites of  
2 claim 1 wherein the  $\beta$ -glucan compound is derived from one of bacteria,  
3 yeast, and fungi.

1 21. The medical composition for application to wounds and to surgical sites of  
2 claim 1 wherein the medical composition comprises one of the inorganic silver  
3 salts.

1 22. The medical composition for application to wounds and to surgical sites of  
2 claim 1 wherein the medical composition comprises one of the organic silver  
3 salts.

1 23. The medical composition for application to wounds and to surgical sites of  
2 claim 18 further including a viscosity agent and a preservative agent, the  
3 preservative agent comprising one or more of the group comprising:

4	methyl paraben	0.05 – 3 w/w%
5	propyl paraben	0.001 – 1 w/w%
6	benzylalkonim chloride	10 – 200 ppm
7	ethyl paraben	100 - 3000 ppm
8	imidurea	500 - 10,000 ppm
9	diazolidinyl urea	500 – 10,000 ppm.

1 24. The medical composition of claim 9, wherein said topical composition is one  
2 of a cream and a lotion and comprises:  
3 a cereal-derived  $\beta$ -glucan;  
4 a solvent including water;  
5 an ointment base;  
6 an emulsifying/solubilizing agent;  
7 a suspending/viscosity increasing agent; and,  
8 a preservative agent.

1 25. The medical composition of claim 24, wherein said solvent comprises at least  
2 20 w/w percent of said topical composition.

1 26. The medical composition of claim 24, wherein said ointment base comprises  
2 about 3 - 60 w/w percent of said topical composition.

1 27. The medical composition of claim 24, wherein said ointment base comprises  
2 one or more of cod liver oil, mineral oil, shark liver oil, paraffin, petrolatum,  
3 lanolin, cetyl alcohol, and cetyl esters wax.

- 1 28. The medical composition of claim 24, wherein said emulsifying/solubilizing  
2 agent is selected from a group including sodium lauryl sulfate and non-ionic  
3 emulsifiers such as glyceryl stearate, PEG 100 stearate and triethanolamine.
- 1 29. The medical composition of claim 24, wherein said suspending/viscosity  
2 increasing agent is selected from the group comprising polyvinyl alcohol,  
3 agarose, alginate, xanthan gum, carrageenan, guar gum, sodium  
4 carboxymethylcelluloses, and carbomer.
- 1 30. The medical composition of claim 24, wherein said preservative agent is  
2 selected from the group comprising methyl paraben, ethyl paraben, butyl  
3 paraben, propyl paraben, benzalkonium chloride, imidurea, and diazolidinyl  
4 urea.
- 1 31. The medical composition of claim 9, wherein said topical composition is one  
2 of a cream and a lotion and comprises:  
3 cereal-derived  $\beta$ -glucan;  
4 a solvent;  
5 an emulsifying/solubilizing agent;  
6 a suspending/viscosity increasing agent; and,

7           a preservative agent.

1   32.   The medical composition of claim 9, wherein said topical composition is a gel  
2           having a gel base including water and at least one suspending/viscosity  
3           increasing agent.

1   33.   The medical composition of claim 9, wherein said topical composition is a gel  
2           having a water base including at least about 50 w/w percent water.

1   34.   The medical composition of claim 32, wherein said medical composition  
2           includes:  
3           water - about 50 - 98 w/w percent  
4           suspending/viscosity increasing agent(s) - about 0.5-15.0 w/w percent.

1   35.   The medical composition of claim 34, wherein said suspending/viscosity  
2           increasing agent(s) comprises at least one of a group including polyvinyl  
3           alcohol, carboxymethylcelluloses, alginate, carrageenan and xanthan gum.

1   36.   The medical composition of claim 34, wherein said suspending/viscosity  
2           increasing agents comprise polyvinyl alcohol plus one other.



- 1 37. The medical composition of claim 34, further comprising a preservative agent.
- 1 38. The medical composition of claim 36, wherein said one other  
2 suspending/viscosity increasing agent comprises one of xanthan gum,  
3 agarose, alginate, guar gum, carboxymethylcellulose, and carbomer.
- 1 39. A medical composition for application to skin and mucosa for burns and  
2 wounds and other skin loss injuries and conditions comprising cereal-derived  
3  $\beta$ -glucan and a silver compound as active ingredients in one of a cream base,  
4 gel base and oil base.
- 1 40. The medical composition of claim 39, wherein said cereal derived  $\beta$ -D-glucan  
2 is derived from one of oats, wheat and barley.
- 1 41. The medical composition of Claim 39 wherein the silver compound is one of  
2 silver nitrate, silver bromide, silver sulfate, silver fluoride, silver iodide, silver  
3 chloride, silver oxides, silver protein, silver lactate, silver citrate, or silver  
4 sulfadiazine.

- 1 42. The medical composition of claim 39, wherein said cereal derived  $\beta$ -glucan is  
2 derived from oats.
- 1 43. The medical composition of claim 39, wherein said cereal derived  $\beta$ -glucan is  
2 characterized as (1 $\rightarrow$ 3)(1 $\rightarrow$ 4)  $\beta$ -glucan.
- 1 44. The medical composition for application to skin and mucosa for burns and  
2 wounds and other skin loss injuries and conditions of claim 39 wherein the  
3 medical composition comprises one of the organic silver salts.
- 1 45. The medical composition for application to skin and mucosa for burns and  
2 wounds and other skin loss injuries and conditions of claim 39 wherein the  
3 medical composition comprises one of the inorganic silver salts.
- 1 46. A topical composition for treating burns, wounds, and scarring of the skin and  
2 mucosa, wherein said composition contains 0.05-15 w/w % cereal-derived  $\beta$ -  
3 glucan and a silver compound, said composition selectively formulated as one  
4 of the group comprising an unguent, cream, gel, emollient, oil and lotion.
- 1 47. A biocompatible surgical mesh for implantation at a surgical site having  
2 applied thereto a medical composition comprising a  $\beta$ -glucan compound and  
3 one of elemental silver and a silver compound.

- 1 48. The biocompatible surgical mesh for implantation at a surgical site of Claim 47  
2 wherein the silver compound of the medical composition is one of silver  
3 nitrate, silver bromide, silver sulfate, silver fluoride, silver iodide, silver  
4 chloride, silver oxides, silver protein, silver lactate, silver citrate, or silver  
5 sulfadiazine.
- 1 49. The biocompatible surgical mesh for implantation at a surgical site of claim 47  
2 wherein the beta D glucan compound is derived from one of oats, barley, or  
3 wheat.
- 1 50. The biocompatible surgical mesh for implantation at a surgical site of claim 47  
2 wherein the beta D glucan composition is derived from one of yeast, bacteria,  
3 and fungus.
- 1 51. The biocompatible surgical mesh for implantation at a surgical site of claim 47  
2 wherein the surgical mesh is fabricated from a material chosen from a group  
3 comprising polyester, polypropylene, polytetrafluoroethylene, expanded  
4 polytetrafluoroethylene, polyethylene terephthalate, polyglycolic acid,  
5 polyglactin, and dacron-polythene reinforced silicone.

- 1 52. The biocompatible surgical mesh for implantation at a surgical site of claim 47  
2 wherein the surgical mesh is organic and is derived from one of a human  
3 source, an animal source, and a cadaveric source.
- 1 53. The wound dressing of claim 53 wherein the medical composition comprises  
2 one of the organic silver salts.
- 1 54. The wound dressing of claim 53 wherein the medical composition comprises  
2 one of the inorganic silver salts.
- 1 55. A wound dressing comprising a mesh material and a coating on said mesh  
2 material comprising a medical composition including a  $\beta$ -glucan compound  
3 and one of elemental silver and a silver compound.
- 1 56. The wound dressing of Claim 55 wherein the silver compound of the medical  
2 composition is one of silver nitrate, silver bromide, silver sulfate, silver  
3 fluoride, silver iodide, silver chloride, silver oxides, silver protein, silver lactate,  
4 silver citrate, and silver sulfadiazine.
- 1 57. The wound dressing of claim 55 wherein the  $\beta$ -glucan compound is derived  
2 from one of oats, barley, or wheat.

- 1 58. The wound dressing of claim 57 wherein the  $\beta$ -glucan comprises about 0.01 –  
2 15 w/w% of the wound dressing.
- 1 59. The wound dressing of claim 55 wherein the  $\beta$ -glucan composition is derived  
2 from one of yeast, bacteria, and fungus.
- 1 60. The wound dressing of claim 55 wherein the  $\beta$ -glucan composition comprises  
2 about 0.01 – 15 w/w% of the wound dressing.
- 1 61. The wound dressing of claim 55 wherein the mesh material is fabricated from  
2 a material chosen from a group comprising polyester, polypropylene,  
3 polytetrafluoroethylene, expanded polytetrafluoroethylene, polyethylene  
4 terephthalate, polyglycolic acid, polyglactin, and dacron-polyethylene  
5 reinforced silicone.
- 1 62. The wound dressing of claim 55 wherein the mesh material is organic and is  
2 derived from one of a human source, an animal source, and a cadaveric  
3 source.
- 1 63. The wound dressing of claim 55 wherein a polymeric vapor permeable film is  
2 applied to one side of the mesh material.

- 1 64. The wound dressing of claim 55 wherein the medical composition further  
2 comprises 0.1 – 20 w/w% (dry weight) of a collagenic protein.
- 1 65. The wound dressing of claim 55 wherein the medical composition comprises  
2 one of the organic silver salts.
- 1 66. The wound dressing of claim 55 wherein the medical composition comprises  
2 one of the inorganic silver salts.
- 1 67. A wound dressing comprising:  
2 a polyester mesh netting formed of woven monofilament polyester and having  
3 a netting thickness of about 0.01-0.05 inches;  
4 a coating on said mesh netting filaments comprising a medical composition  
5 including an oligosaccharide and a silver compound that is mixed with  
6 a collagenic protein in a ratio of 1:100 to 100:1 (dry basis); and  
7 a polymeric film of high vapor permeable material bonded to one side of the  
8 coated mesh netting to comprise an exterior surface of said wound  
9 dressing.

- 1 68. The wound dressing of claim 67, wherein said polymeric film comprises a  
2 stabilized butylene/poly(alkylene ether) phthalate material.
- 1 69. The wound dressing of claim 67, wherein said oligosaccharide of said medical  
2 composition comprises a  $\beta$ -glucan compound and said collagenic protein  
3 comprises a bovine hide extract including Type I and Type III collagens.

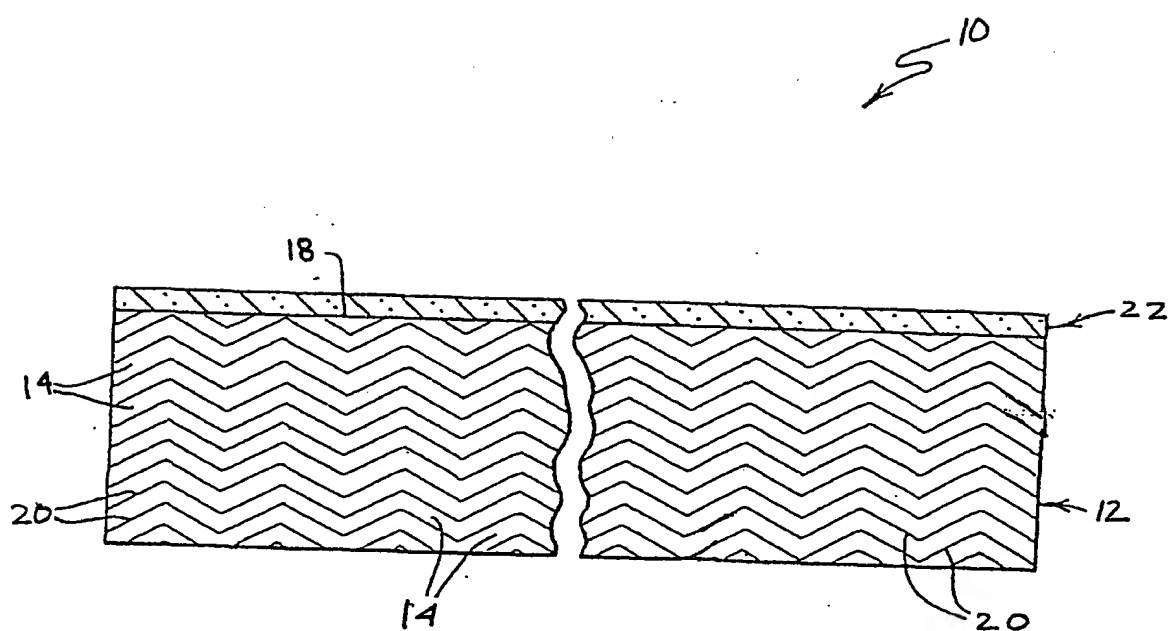


FIG. 1



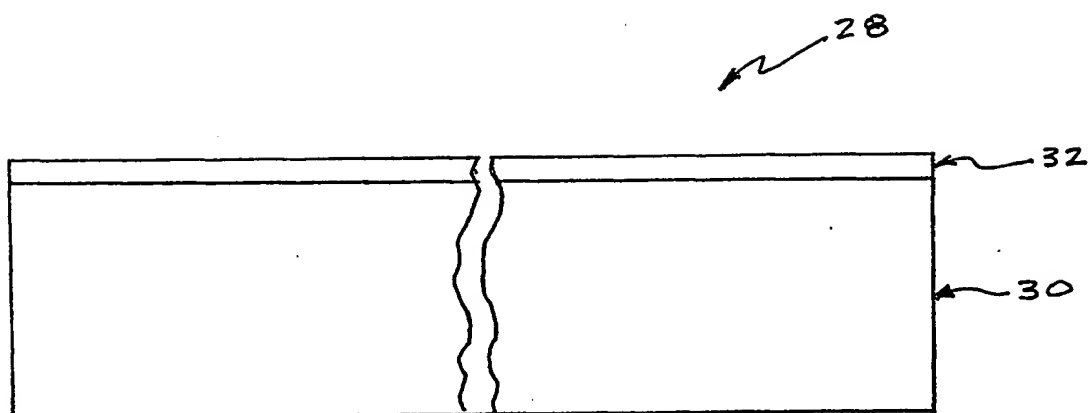


FIG. 2

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/08741

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 6/00, 7/00, 9/70; A61F 13/00; A61L 15/16, 15/00

US CL : 424/401, 443, 445, 446, 447; 514/969

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/401, 443, 445, 446, 447; 514/969

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

BRS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,158,772 A (DAVIS) 27 October 1992 see entire document.	1-69
Y	US 5,676,967 A (WILLIAMS et al) 14 October 1997 see entire document.	1-69
Y	US 5,980,918 A (KLEIN) 09 November 1999, see entire document.	1-69
Y	US 4,803,066 A (EDWARDS) 07 February 1989 see entire document.	1-69
Y	US 5,326,567 A (CAPELLI) 05 July 1994 see entire document.	1-69

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

14 JUNE 2001

Date of mailing of the international search report

02 AUG 2001

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer  
TODD D WARE

Telephone No. (703) 308-1235